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ptilomycalin A (1,  $R^1 = R^2 = R^3 = H$ ; n = 1) crambescidin 800 (2,  $R^1 = R^3 = H$ ,  $R^2 = OH$ ; n = 1) crambescidin 816 (3,  $R^1 = R^2 = OH$ ,  $R^3 = H$ ; n = 1) crambescidin 830 (4,  $R^1 = R^2 = OH$ ,  $R^3 = H$ ; n = 2) crambescidin 844 (5,  $R^1 = R^2 = OH$ ,  $R^3 = H$ ; n = 3) celeromycalin (6,  $R^1 = R^2 = H$ ;  $R^3 = OH$ ; n = 1)

13, 14, 15 - isocrambescidin 800 (10)

B OH NH2

fromiamycalin (9)

R = H(7)R = allyf(8)

13, 14, 15 - isocrambescidin 657 (10a)

Figure 1

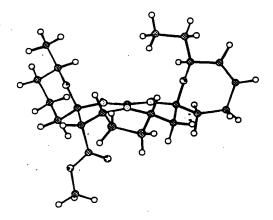


Figure 2

HOC ROOF ITEMS

ROOF ITEMS

$$X = 0 \text{ or NR}$$
 $X = 0 \text{ or NR}$ 
 $X = 0 \text{ or NR}$ 

FIGURE . 3

substrate	reaction conditions	17:18 (yield) <sup>4</sup>	
1.8	morpholinium acetate (1.5 eq),	4:1 (80%)	
15	CF <sub>3</sub> CH <sub>2</sub> OH, 60 °C, 48 h	4:1 (81%)	
15	PPE, CH <sub>2</sub> Cb, 23 °C, 48 h	1:4 (60%)	

<sup>\*</sup> Combined overall yield of 17 and 18 from 14.

#### FIGURE 4

FIGURE 5

265

265

CF3CH2OH, 60 °C, 48 h

PPE, CH2Ch, 23 °C, 48 h

7:1 (84%)

1:20 (61%)

FIGURE 6

<sup>&</sup>lt;sup>4</sup> Combined overall yield of 27 and 28 from 25.

#### iminium ion pathway

$$X = 0 \propto NSO_2Ar$$

$$+16, -HY$$

$$X = 0 \propto NSO_2Ar$$

$$+16, -HY$$

$$7$$

$$29$$

$$(X = 0, NSO_2Ar, NH2*)$$

#### FIGURE 7

Figure 8

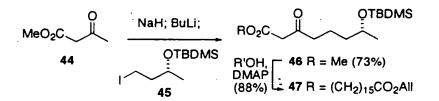


Figure 9

Figure 10

Figure 11

Figure 12

Figure 13

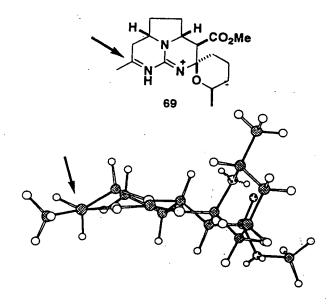


Figure 14

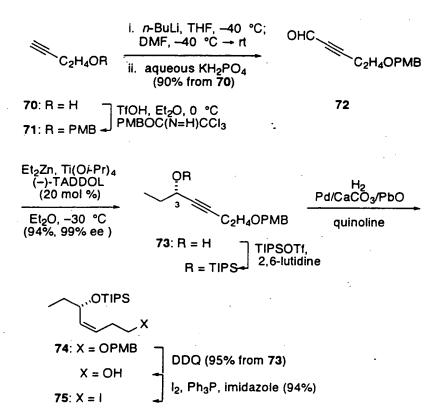


Figure 15

Figure 16

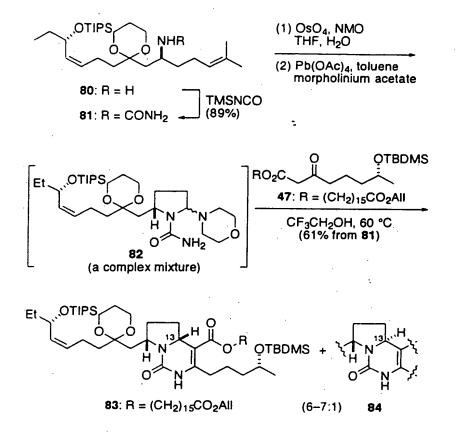


Figure 17

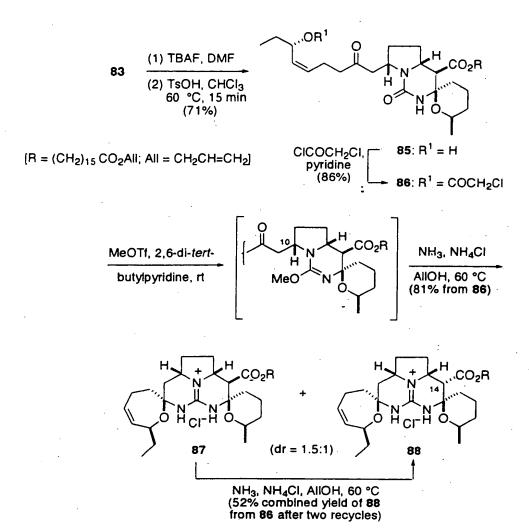


Figure 18

Figure 19

13,14,15-isocrambescidin core

crambescidin/ptilomycalin A core

Figure 21

Figure 22

Figure 23

Figure 24

 $\mathsf{R} = (\mathsf{CH}_2)_{15} \mathsf{CO}_2 \mathsf{AII}$ 

 $^{\rm a}{\rm Reagents}$ : (a) PPTS, CHCl3, 90 °C, 24 h; HCO2 Na wash or 0.1 N HCl wash

Figure 25

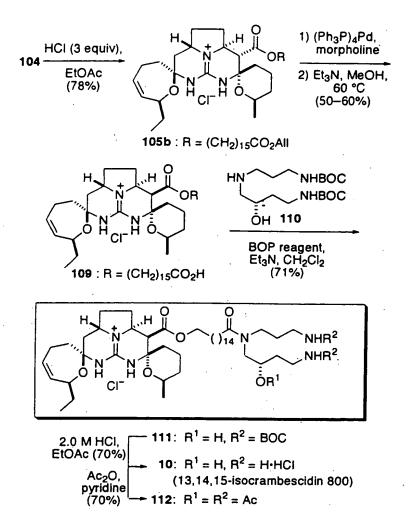


Figure 26

Figure 27

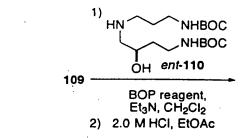


Figure 28

synthetic 10
117
natural 10

R-MTPA-CI, Et<sub>3</sub>N
DMAP, CH<sub>2</sub>CI<sub>2</sub>

entry	starting material	product	<sup>19</sup> F NMR (CDCl <sub>3</sub> ) <sup>a</sup> , δ ppm
1	synthetic 10	118	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9
2	117	119	-68.6, -68.7, -68.8, -68.9, -71.071.1
3	natural 10	118	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9

<sup>&</sup>lt;sup>a</sup>Due to rotamers about the C38 amide, there are six peaks in the <sup>19</sup>F NMR spectra.

Figure 29

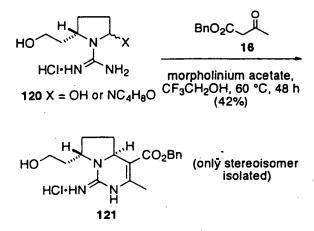
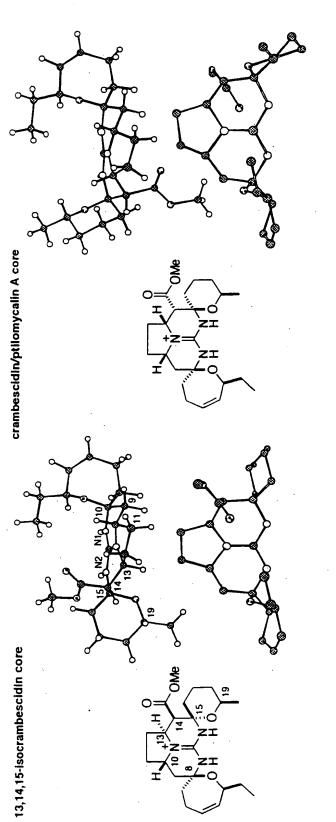


Figure 30



123 (only stereoisomer isolated; 42% over 3 steps)

Figure 32

Figure 33

Figure 34

$$\mathsf{R} = (\mathsf{CH}_2)_{15} \mathsf{CO}_2 \mathsf{All}$$

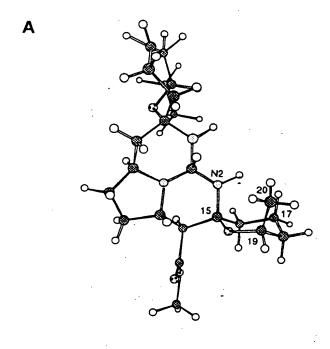
Figure 35

 $R = (CH_2)_{15}CO_2AII$ 

 $^{\rm a}{\rm Reagents}\colon$  (a) PPTS, CHCl3, 90 °C, 24 h; HCO2Na wash or 0.1 N HCl wash

Figure 36

Figure 37



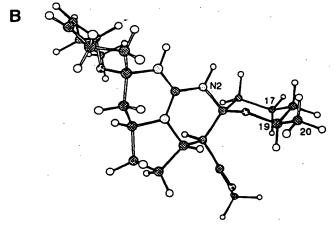


Figure 38

Figure 39

Figure 40

Figure 41

Figure 42

Figure 43

entry	starting material	product	<sup>19</sup> F NMR (CDCl <sub>3</sub> ) <sup>a</sup> , δ ppm
1	synthetic 10	148.	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9
2	147	149	-68.6, -68.7, -68.8, -68.9, -71.071.1
3	natural 10		-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9

 $<sup>^{\</sup>rm a}{\rm Due}$  to rotamers about the C38 amide bond on the NMR time scale , six peaks are observed in the  $^{\rm 19}{\rm F}$  NMR spectra.

Figure 44

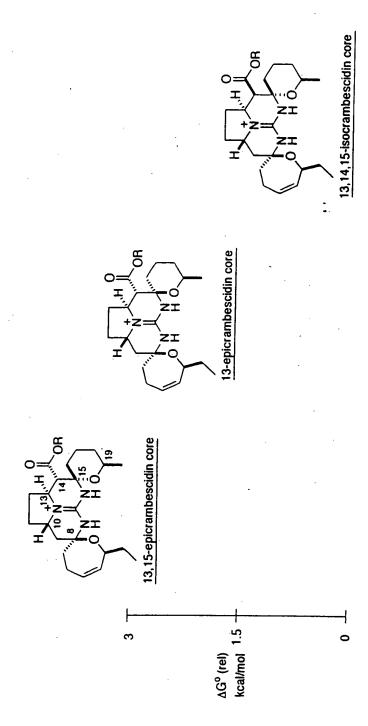


Figure 46

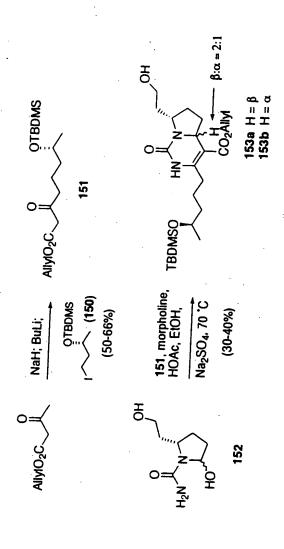


Figure 48

Figure 49

Figure 50

Figure 52

 $[AII = CH_2CH=CH_2]$ 

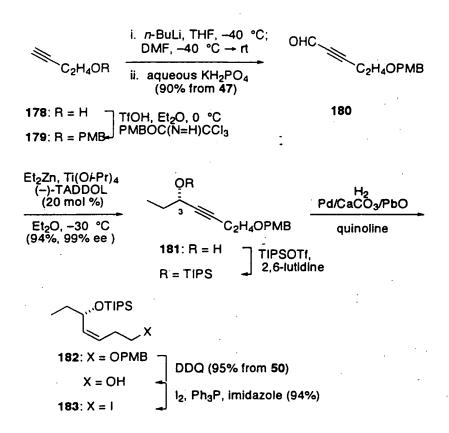


Figure 53

Figure 54

Figure 55

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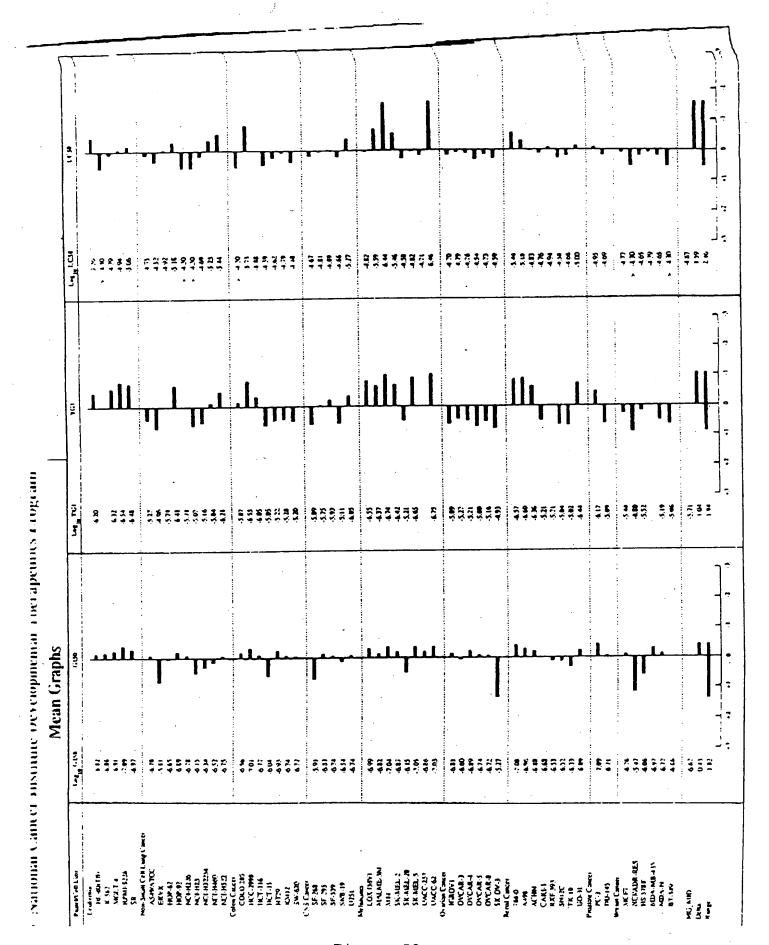
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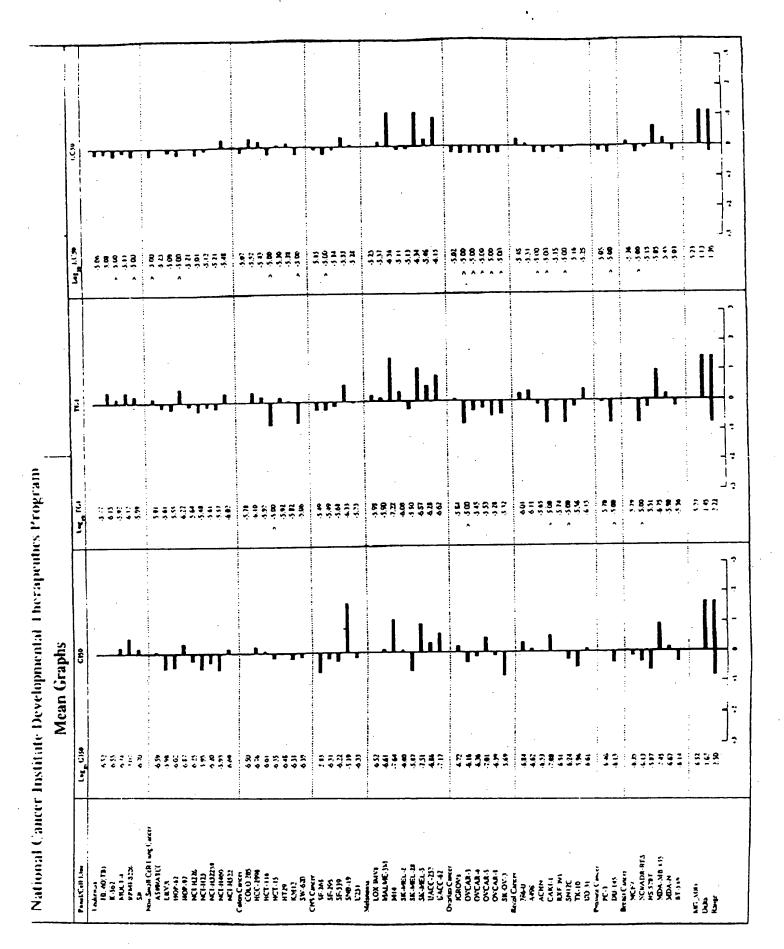
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Figure 57

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Figure 62